Date: May 15, 2018

Clinical Protocol: Migraine

PREAMBLE

- Consider more sinister causes for headache
- Red flags
  - Change in previously existing headache (intensity, frequency, pattern)
  - Daily or continuous headache
  - Effort-related or positional headache
  - Headache associated with change of personality or mental status
  - Headache brought on by coughing, sneezing, or bending
  - Headache brought on by exercise or orgasm
  - Headaches awakening from sleep
  - Headaches that become refractory to previously effective treatment
  - Jaw pain (claudication)
  - Migraine aura that begins or persists after the headache has dissipated
  - New onset after age 50 years
  - Previous head trauma
  - Rapidly increasing headache frequency
  - Subjective numbness or tingling inconsistent with sensory aura of migraine
  - Sudden explosive onset of headache with rapid progression over seconds to minutes
  - Worsens with the Valsalva maneuver
  - Worst headache of life
- Consider medication overuse headaches in the differential
  - Associated with dose frequency rather than the absolute quantity of drug
  - Suspect in patients with 10 – 15 or more headaches per month
  - Headaches may be tension type or migraine-like
- Treatment is divided into:
  - Acute Migraine Therapy
  - Prophylactic Migraine Therapy
  - Perimenstrual Migraine Therapy
  - Perimenopausal Migraine Therapy
- Patients with ME/CFS may need to have medication titrated more slowly, and may not tolerate higher doses
- The treatments described below may occur one-on-one or in a group setting depending on resources
- Provide patient with information/dose adjustment handout
- It is expected that physicians would educate themselves about these drugs beyond the outline provided below

1. Patient Education

- RCT data
- Improves compliance and reduces headache activity
- Patients should keep a log/diary of headache severity, associated disability, and response to treatments

- Incorporated into multiple offerings (e.g., handouts, web-based resources)
- Incorporated into core group: Living with Complex Chronic Diseases
- "Family and Friends" evening session
- Incorporated into other groups

2. Physical Activity

- Level A evidence
- Offered in group setting and individual sessions with PT and OT
- Tai-Chi and mild Yoga
  - Suggested
  - Offerings in community rather than CCDP

3. Sleep

- RCT data
- Too little or too much sleep can be a problem
- Sleep disturbance can be a major trigger for migraines
- See sleep protocol for details

4. Diet

- RCT data
- Most important dietary triggers are delayed or missed meals
- Specific dietary triggers are associated in some individuals
  - In particular, reduced intake of caffeine, artificial sweeteners, and additives (such as monosodium glutamate)
- Offered in group setting and individual sessions with dietitian

5. Alterative and Complementary Therapies

- RCT and meta-analysis data

5.1 Petasites (butterbur root extract)

- Level A evidence
- For migraine prophylaxis
- Watch for GI upset, eructation, and elevation of liver enzymes
- Can interact with medications that induce cytochrome P450 (i.e., carbamazepine, Phenobarbital, phenytoin, rifampin, rifabutin and other)
- 75 mg BID

5.2 Feverfew (MIG-99)

- Level B evidence
- For migraine prophylaxis
- Generally well tolerated, but watch out for GI symptoms, mouth ulcerations and post feverfew syndrome (rebound migraine, anxiety, insomnia)
- May inhibit cytochrome P450 isoenzymes and may have drug interactions with prescription medications; use with caution

- May inhibit platelet aggregation; therefore, may increase the risk of bleeding when used with anti-coagulants/anti-platelet medications
- 6.25 mg TID

5.3 High-dose riboflavin (vitamin B2)

- Level B evidence
- For migraine prophylaxis
- Adverse effects: diarrhea, polyuria; discoloration of urine
- 400 mg daily or 200 mg BID

5.4 Magnesium malate

- Level B evidence
- Watch for diarrhea; GI upset; reduce dose as tolerated
- 250 mg QID

5.5 Co-Q10

- Level C evidence
- Adverse effects: GI upset
- 100 mg TID

6. Psychological and Behavioural Therapies

- RCT data (30-50% reduction in frequency)
- Incorporated in core group: Living with Complex Chronic Diseases
  - Combines Education, Pacing, CBT &, Mindfulness
  - 10 weekly
- One-on-one counselling
- Incorporated into other groups

7. Interventions

7.1 Trigger Point Injection, etc.

- Emerging evidence and expert opinion
- Maneuvers that resolve muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions
- For example:
  - Myofascial release
  - Trigger Point Injections
  - Nerve blocks
- Currently available at:
  - Internally
  - Externally (outside referral):
    - Change Pain Clinic
    - Muscle MD
    - Myo Clinic (Victoria)
    - Other practitioners across the province

7.2 Acupuncture

- RCT data

8. Medications

ACUTE MIGRAINE THERAPY

8.1 NSAIDS

- RCT and meta-analysis data
- Level B evidence
- Mild to moderate migraines
- More effective if taken at onset of headache (abortive treatment)
- Large single dose tends to work better than repetitive small doses
- Use usual cautions when prescribing NSAIDs

8.1 A Ibuprofen

- 400 – 800 mg q4h
- Max 2400 mg/day
- Rapid absorption and onset of action but short duration of action
- Solubilized (gel caps) has a higher response rate for relief

8.1 B Naproxen sodium

- 500-550 mg BID
- Max 1375 mg/day

8.1 C Diclofenac

- 50 – 100 mg TID
- Max 150 mg/day
- Rapid absorption and onset of action but short duration of action

8.1 D Acetylsalicylic acid (ASA tab)

- 975-1000 mg Q4-6h
- Max: 2600 mg/day

8.2 Antiemetics

- RCT data
- Added when nausea is prominent

8.2 A Metoclopramide

- 10 – 40 mg Q4-6h

8.3 Triptans

- RCT and meta-analysis data (level A)
- First line for severe migraines
- More effective if taken at onset of headache (abortive treatment)

- Large single dose tends to work better than repetitive small doses
- Highest likelihood of consistent success was found with Rizatriptan
- Combined use of a triptan and NSAID more effective than either drug class alone
- Contraindicated in patients with:
  - Known or suspected vasospastic or ischemic vascular disorders
  - Uncontrolled hypertension
  - Rare migraine sub-types
    - Hemiplegic migraine
    - Basilar migraine
- Watch for:
  - Limb heaviness
  - Flushing
  - Paresthesia
  - Tightness in the chest, neck, or throat
  - Hypertension
- These side effects can usually be mitigated with lower dose or switching triptans
- Combination with SSRI/SNRI does not significantly increase risk for serotonin syndrome
- Below are the currently available triptans eligible as a Pharmacare benefit (benefits for Groups BCFU)
- The patient's response to one triptan versus another cannot be predicted; therefore, it may be necessary to trial different triptans
- Tablet formulation can play a significant role in efficacy in some patients

8.3 A Rizatriptan (available as orally disintegrating tablets and oral tablets)

- Fastest onset of action
- Usual dose: 5 – 10 mg
- May repeat dose after 2 hrs
- Max 20 mg/day

8.3 B Zolmitriptan (available as nasal spray and orally disintegrating tablets)

- Usual dose: 2.5 – 5 mg
- May repeat dose after 2 hrs
- Max 10 mg/day

8.3 C Almotriptan (available as oral tablets)

- Usual dose: 6.25-12.5 mg
- May repeat after 2 hrs
- Max 25 mg/day

8.3 D Naratriptan (available as oral tablets)

- Usual dose: 2.5 mg
- May repeat after 4 hours
- Max: 5 mg/day

8.3 E Sumatriptan

- **Nasal**
  - Usual dose: 20 mg
  - May repeat dose after 2 hours
    Max: 40 mg/day

- **Oral Tablets/ODT**
  - Usual dose: 50-100 mg
  - May repeat after 2 hours
  - Max: 200 mg/day

- **Subcutaneous Injection** (requires Special Authority for coverage)
  - Usual dose: 6 mg
  - May repeat after 2 hours
  - Max: 12 mg/day

8.4 Opioids

- Should not be used for migraines, except as a last resort
- Use of opiates should not exceed 2 doses per week
- More frequent use may lead to medication overuse headaches

8.5 Combination triptan / NSAID

- May be considered for patients who do not respond well to triptan alone
- Usual combinations are with sumatriptan-naproxen

8.6 Dihydroergotamine (available as intranasal and subcutaneous injections)

- Subcutaneous
  - 1 mg S/C; may repeat at 1 hr intervals for a Max daily dose of 3 mg
  - Max 6 mg/week
- Nasal Spray
  - 0.5 mg into each nostril. May repeat after 15 min
  - Max 4 sprays

PROPHYLACTIC MIGRAINE THERAPY

- Consider in:
  - Recurrent headaches that interfere with daily routine
    - Usually at least 2/month
  - Contraindication to acute therapy
  - Failure or overuse of acute therapy
  - Adverse effects from acute therapy
  - Patient preference
  - Uncommon migraine (e.g., basilar- type, hemiplegic)
- Expect a 33 – 55% reduction in frequency and a reduction in severity
- RCT and meta-analysis data
- Evidence is strongest (Level A) for propranolol, topiramate, metoprolol, and divalproex
- Level B evidence for amitriptyline, and venlafaxine
- Calcium channel blockers are no longer considered effective

- Titrated upward over a few weeks and then sustained for 4–8 weeks before benefit is realized

8.7 Propranolol

- Use usual cautions when prescribing beta-blockers
- Small doses may also benefit patients with POTS (up to 40 mg/day)
- Patients with POTS do not usually tolerate higher degree of beta blockade
- Usual dose 40 – 160 mg/day
- 20 – 80 mg BID

AM	PM	
10 mg		1 weeks
10 mg	10 mg	1 weeks
20 mg	10 mg	1 weeks
20 mg	20 mg	Stay at this dose for 4 – 8 weeks, then reassess
Use same schedule to increase if needed and as tolerated		

- *When patient is using rizatriptan, reduce the dose of rizatriptan by half and maintain a gap of 2 hours between intake of rizatriptan

8.8 Topiramate

- Also helpful for pain in FM and other conditions
- See FM protocol for more details
- Usual dose 25-200 mg/day
- Doses above 100 mg/day tend to have more adverse effects

8.9 Metoprolol

- Use usual cautions when prescribing beta-blockers
- Small doses may also benefit patients with POTS (25 mg BID)
- Patients with POTS do not usually tolerate higher degree of beta blockade
- Usual dose 50- –200 mg/day
- 50 – 100 mg BID

AM	PM	
12.5 mg		1 weeks
12.5 mg	12.5 mg	1 weeks
25 mg	12.5 mg	1 weeks
25 mg	25 mg	1 weeks
25 mg	37.5 mg	1 weeks
37.5 mg	37.5 mg	1 weeks
37.5 mg	50 mg	1 weeks
50 mg	50 mg	Stay at this dose for 4 – 8 weeks, then reassess
Use same schedule to increase if needed and as tolerated May use XL (extended release) form as a single daily dose instead		

8.10 Valproate/Divalproex

- Watch for: nausea, somnolence, weight gain, hepatitis, pancreatitis
- Monitor liver tests and CBC (neutropenia):
  - baseline, then q month x 6, then q 6 month

- Teratogenic risk
  - Should not be used in women of childbearing age
- Usual dose 500 – 1000 mg/day

AM	PM	
125 mg		2 weeks
125 mg	125 mg	2 weeks
250 mg	125 mg	2 weeks
250 mg	250 mg	Stay at this dose for 4 – 8 weeks, then reassess
Use same schedule to increase if needed and as tolerated May use divalproex (extended release) form as a single daily dose instead		

8.11 Amitriptyline

- Also helpful for pain in FM and other conditions
- See protocol: Pain in Fibromyalgia, ME/CFS, and related disorders: Pharmacologic

8.12 Venlafaxine

- Also helpful for pain in FM and other conditions
- See protocol: Pain in Fibromyalgia, ME/CFS, and related disorders: Pharmacologic

8.13 Botox

- For patients with more than 15 headaches per month (chronic migraine)
- RCT data

PERIMENSTRUAL MIGRAINE THERAPY

- Can be prevented by perimenstrual (2 days before, continuing for 6 days) frovatriptan

8.14 Frovatriptan

- Level A evidence
- 2.5 mg twice daily

Perimenopausal Migraine Therapy

- For some, perimenopause brings relief of migraine intensity and frequency; for others, migraines are exacerbated during this time
- Both hormonal and non-hormonal therapy (i.e., fluoxetine and venlafaxine) are effective: RCT data and guidelines
  - See FM protocol for venlafaxine dosing and recommendations

HORMONE THERAPY (HT)

- HT can benefit migraines, but in some, migraines are worsened
- Before considering hormone therapy do a risk assessment
  - Smoking
  - Family and medical history

  - Deep vein thrombosis
  - Breast cancer
  - Cardiovascular disease including TIA/stroke
- Perimenopausal migraines are exacerbated by hormone fluctuations
  - HT via transdermal patch or gel delivers a more consistent dose of hormones than does oral medication, and is more effective while reducing side effects
- HT may be helpful in women who also have significant vasomotor symptoms
- Use only the lowest doses necessary to control symptoms minimize side effects

8.15 Hormone Therapy

- Refer to GP for implementation

9. Assess and Treat Coexisting Central Sensitivity Syndromes

- Level A evidence for most of these conditions
- May require referral out
- Central Sensitivity Syndromes include:
  - ME/CFS
  - FM
  - IBS
  - Migraine
  - Tension Type Headaches
  - POTS (Postural Orthostatic Tachycardia Syndrome)
  - Multiple Chemical Sensitivities
  - Interstitial Cystitis
  - Pelvic Pain Syndromes
  - Irritable Larynx Syndrome
  - Restless Leg Syndrome
  - Temporomandibular Disorders
  - Myofascial Pain Syndrome
  - PTSD

10. Assess and Treat for Coexisting Anxiety and Mood Disorders

- Level A evidence
- Referral to psychiatrist for selected patients

Patient Resources :
http://www.bcwomens.ca/health-info/living-with-illness/living-with-complex-chronic-disease/migraines